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Balancing Hydrogen Bonding and van der Waals Interactions in Cyclohexane-Based Bisamide and Bisurea Organogelators†

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The solvent dependence of the gelation properties, the thermotropic behavior, and the melting enthalpy of a series of enantiomerically pure cyclohexane-based bisamide and bisurea compounds are reported. The two series of gelators examined are related structurally with the intermolecular interactions responsible for gelation differing in a systematic manner through varying the length of the alkyl tail and the number of hydrogen bonding units present. The gelation properties of the compounds in decalin, DMSO, and 1-propanol were studied by FTIR spectroscopy and by comparison of the thermal stability of their gels as determined by dropping ball experiments and by differential scanning calorimetry (DSC). FTIR spectroscopy, supported by the single-crystal X-ray diffraction of **a3**, indicates that the gelator molecules are aggregated through intermolecular hydrogen bonding in all of the solvents examined. The thermal stability of the gels in apolar and polar solvents was found to be dependent primarily on the relative strength of intermolecular hydrogen bonding and van der Waals interactions, respectively, compared with the strength of solvent−gelator interactions. The results of DSC indicated that the contribution of the difference in intergelator van der Waals interactions, compared with the gelator−solvent van der Waals and hydrogen bonding interactions, provided by the alkyl tail to the stability of the gel has a linear relationship with the number of methylene units in alkyl chains of length greater than six. In polar solvents, this contribution lies between 3.5 and 4.2 kJ mol^{-1} per methylene unit, and in apolar solvents, it is 2.2 kJ mol^{-1}. The hydrogen bonding interactions were weaker in polar solvents and hence gelation occurred only where sufficient compensation was provided by intergelator van der Waals interactions. The results show that the direct relation of gelation strength to changes in solvent properties is not possible and more complex relationships should be considered. Furthermore, it is apparent that the development of design rules for the construction of LMWG molecules incorporating more than one anisotropic growth element must take into consideration the role of the solvent in determining which of the contributions is dominant.

Introduction

Gelation, the trapping of a liquid by a network of fibers,[1] is a remarkable phenomenon, not least in the case of low-molecular-weight gelators (LMWGs). These LMWGs typically form a network of supramolecular fibers through the anisotropic aggregation of individual molecules; therefore, the formation of gels by LMWGs is an excellent phenomenon for furthering the understanding of the mechanisms involved in supramolecular self-assembly, which is one of the major challenges in modern science.[2] The number of polymeric, inorganic, and LMWG systems capable of gelating both polar and apolar solvents is increasing steadily;[3−7] concomitantly, our understanding of the forces that drive gelation (e.g., ion−ion, dipole−dipole, magnetic dipole−dipole,[8] hydrogen bonding, van der Waals, and $\pi-\pi$ stacking interactions) is increasing.[9−13]

There are several ways that these LMWGs form gels: via platelets,[14,15] via colloids,[16] or via fibrillar material.[4] In the case of LMWGs that form a fiber network, a central aspect that has been deemed essential in the formation is the anisotropy of the intermolecular interactions responsible for the growth of aggregates in one dimension.[3,4,17] Once formed, these fibers interact to form part of a 3D network that traps the solvent and leads to what is recognized at the macroscopic level as a gel. A key challenge in the rational design of LMWGs is to understand the level and nature of (anisotropic) intermolecular interactions that are required to achieve gelation and the relative contributions that are made by the various intermolecular interactions and how the solvent itself affects these contributions and hence the strength of

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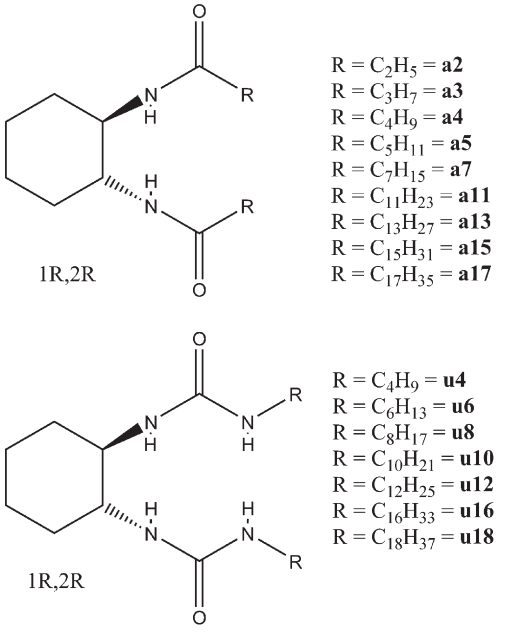

Figure 1. Cyclohexane-based bisamide organogelators **a2** to **a17** and bisurea organogelators **u4** to **u18** employed in this study.

the gel fibers formed.[12] Already some attempts have been made to further the understanding of gelators by X-ray crystal data analysis,[12,18−20] and elaborate studies have been done to design nanoscaled materials with these self-assembled systems.[21]

Here, we focus on the relative contribution of two distinct supramolecular interactions involved in the gelation of solvents by two classes of LMWGs (bisamide- and bisurea cyclohexyl-based gelators (Figure 1)) and on how the solvent influences the contribution of each of these interactions. The molecular scaffold in both series of LMWGs is comparable, hence they provide an excellent handle for understanding the relative contribution of the supramolecular interactions involved in the gelation process. Both systems consist of a cyclohexane framework on which two hydrogen bonding moieties are connected at the 1,2 position in a transoid fashion. The hydrogen bonding motifs (i.e., bisamide and bisurea) are substituted with a linear alkyl tail. These motifs are quite common in the design of LMWGs.[22,23]

The syntheses of bisamide **a11**[24] and bisureas **u4**, **u12**, and **u18**[25] were first reported by Hanabusa et al. in 1996. The ability of bisamides **a7** and **a11** and bisureas **u4**, **u12**, and **u18** to gelate a number of solvents has also been demonstrated.[19,24−26] For both classes, the gelation is presumed to be driven by two different types of intermolecular interactions: van der Waals and hydrogen bonding interactions. The overall sum of these interactions is assumed to lead to an anisotropic aggregation orthogonal to the cyclohexane ring. In the present contribution, we will describe the results of gelation for a series of these systems with respect to their structure, thermal stability, and melting enthalpy. The anisotropy in the system is varied systematically through the length of the *n*-alkyl unit and hence also the contributions of van der Waals interactions and the number of hydrogen bonds (i.e., the bisamide (2 H-bonds) and bisurea gelators (4 H-bonds). The strength of gels in different solvents for each series of LMWGs allows for the role of the solvent, in determining which intermolecular interaction is primarily responsible for the gel fiber formation, to be identified.

Experimental Section

All solvents and reagents for synthesis were reagent grade or better and used as received. Solvents for gelation and spectroscopy were of HPLC or spectrophotometric grade. Bisamide gelators **a2**−**a17** were synthesized as described by Hanabusa et al. for the preparation of bisamide **a11**.[24] One equivalent of (1*R*,2*R*)-(-)-1,2-diaminocyclohexane is coupled with 2 equiv of an alkyl acid chloride using excess of triethylamine in THF at 0 °C. Upon addition of the acid chloride, the reaction mixture becomes viscous, and by heating the reaction mixture at reflux, the aggregates break up. The product is purified by multiple washing steps (the product is only sparely soluble in most organic solvents) and after drying is isolated as a white solid (yields between 32% and 93%). The lower isolated yields are due primarily to the purification procedure.

The synthesis of bisurea gelators **u4**−**u18** was carried out according to the procedure reported earlier for the synthesis of **u12**.[26] One equivalent of (1*R*,2*R*)-(-)-1,2-diaminocyclohexane was coupled to 2 equiv of an alkyl isocyanate in toluene. Immediately after addition of the isocyanate, the reaction mixture became viscous, and the mixture was heated at reflux to break up the aggregates. Purification of the product was performed by multiple washing steps yielding 24−93% of the product as a white powder after drying. Full experimental details and analyses are provided as Supporting Information.

Critical Gelation Concentration (cgc) Determination. The compounds are insoluble at room temperature in most of the solvents examined. Above the critical gelation concentration (cgc), upon heating, they dissolve, and subsequent cooling to room temperature results in the formation of gels. To determine the cgc values for the different compounds, the gels were diluted, heated, and then cooled to room temperature repeatedly until either gels did not form upon cooling or the gels were too weak to withstand gravity. The gels formed were examined after 1 day and 1 week to ensure that aging did not affect the results.

Gel Melting Temperature Determination. Gels were prepared at least 1 day prior to melting experiments. A stainless steel ball with a diameter of 2.5 mm (6.238 mg) was placed on the gels and held at 5 °C h^{-1}, during which its position was monitored[27] via a video camera. The gel was considered to be melted when the ball had reached the bottom of the vial. Dropping-ball experiments were carried out at least in duplicate, and the melting temperatures obtained were reproducible to within ±1 °C.

Single-Crystal X-ray Analysis of a3. Colorless thin platelet-shaped crystals of **a3** were obtained by recrystallization from 1-propanol with slow evaporation of the solvent. A crystal of 0.41 × 0.29 × 0.04 mm^3, although providing only weak X-ray scattering, was sufficient to give a final refinement on F^2 by full-matrix least-squares techniques converged at $wR(F^2)$ = 0.1033 for 1574 reflections and $R(F)$ = 0.0425 for 1324 reflections with $F_o \geq 4.0\,\sigma(F_o)$ and 267 parameters and 1 restraint. Because of the lack of anomalous scatters, absolute structures could not be determined reliably, although on the basis of the starting materials used to prepare **a3** the configuration of C6 and C10 is known to be *R*. For details, see Supporting Information, CCCD reference number CCDC 717396.

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Table 1. Gelation Behavior of Bisamide Gelators with Selected Solvents[a]

solvents[b]	a3	a5	a7	a11	a13	a15	a17	a2	a4
cyclohexane	tg (1.5)	tg (1.1)	tg (2.0)	tg (1.0)	tg (4.5)	tg (0.5)	tg (2.5)	tg (1.5)	c
decalin	cg (2.1)	cg (1.0)	cg (6.0)	cg (4.0)	cg (1.6)	cg (5.0)	cg (4.0)	cg (2.0)	cg (5.0)
di-*n*-butylether	cg (1.9)	cg (3.0)	cg (1.5)	cg (1.5)	cg (2.3)	cg (0.7)	cg (1.5)	cg (2.0)	c
toluene	cg (3.0)	cg (9.0)	cg (5.0)	cg (2.0)	cg (6.0)	cg (4.0)	cg (1.5)	tg (9.0)	tg (3.0)
n-butylacetate	og (15.0)	og (10.0)	tg (6.0)	tg (1.5)	tg (3.0)	tg (1.0)	tg (1.5)	p	og (10.0)
chloroform	s	s	s	s	s	og (5.0)	og (5.0)	s	s
1,2-dichloroethane	c	s	s	tg (4.0)	tg (5.0)	tg (1.5)	tg (2.5)	s	s
dimethylsulfoxide	s	s	tg (5.0)	tg (2.0)	tg (2.0)	tg (3.0)	tg (1.5)	s	s
1-propanol	s	s	p	s[c]	p	tg (2.5)	tg (2.5)	s	s
ethanol	s	s	p	s[c]	p	og (2.5)	og (2.5)	s	s

[a] Abbreviations used: c, formation of microcrystals; cg, clear gel (critical gelation concentration in milligrams of compound per milliliter of solvent); og, opaque gel; tg, turbid gel; i, insoluble at solvent reflux temperature; p, precipitate; s, soluble at room temperature (solubility >20 mg of compound/mL of solvent). [b] The solvents used are listed according to the commonly used $E_T(30)$ scale for solvent polarity.[28] [c] **a11** is soluble up to at least 20 mg/mL, but ref 24 reported gel formation at 33 and 40 mg/mL. However, at the cgc's reported in ref 24, in the present report a precipitate was observed and not a gel.

Table 2. Gelation Behavior of Bisurea Gelators with Selected Solvents[a]

solvents[b]	u4	u6	u8	u10	u12	u16	u18
cyclohexane	i	tg (15.0)	tg (15.0)	tg (2.0)	tg (2.0)	tg (5.0)	tg (1.0)
decalin	c	cg (15.0)	cg (12.0)	cg (10.0)	cg (3.0)	cg (5.0)	cg (7.0)
di-*n*-butylether	i	og (15.0)	tg (10.0)	tg (10.0)	tg (10.0)	tg (5.0)	tg (4.5)
toluene	cg (10.0)	cg (10.0)	cg (10.0)	cg (5.0)	cg (4.0)	cg (4.0)	cg (4.5)
n-butylacetate	c	c	p	og (10.0)	og (10.0)	og (10.0)	og (10.0)
chloroform	c	p	p	p	og (10.0)	og (10.0)	og (10.0)
1,2-dichloroethane	p	p	tg (15.0)	tg (10.0)	tg (1.0)	tg (5.0)	tg (5.0)
dimethylsulfoxide	og (20.0)	og (17.5)	og (7.5)	og (2.5)	og (2.0)	og (0.5)	og (1.0)
1-propanol	p	c	p	og (10.0)	og (2.0)	og (1.5)	og (6.0)
ethanol	c	c	p	og (10.0)	og (3.0)	og (0.8)	og (4.5)

[a] For abbreviations, see Table 1. [b] The solvents used are listed according to the commonly used $E_T(30)$ scale for solvent polarity.[28]

FTIR Spectroscopy. Spectra were recorded on a Nicolet Nexus FTIR instrument. Solid samples were recorded as an intimate mixture with powdered KBr. Liquid and gel samples were recorded in a liquid cell equipped with CaF_2 windows and a 0.2 mm lead spacer.

Differential Scanning Calorimetry. DSC measurements were carried out on a Perkin-Elmer DSC7. A known quantity of gelator together with a known amount of solvent was placed in a 60 μL stainless steel sample cup, which was sealed immediately. The resulting concentrations of gelator are 20−40 mg/mL of solvent. The sample cup was placed in the DSC apparatus together with an empty sample cup as a reference. The cups were heated for 15 min at 20 °C above the melting temperature of the corresponding gel, as determined by the dropping ball technique. Subsequently, the cups were cooled at a rate of 5 °C min^{-1} to 10 °C, where 1-propanol or decalin was employed as the solvent, and to 25 °C, where DMSO was employed as the solvent, at which point the gels formed were allowed to age for 1 h. Heating and cooling scans were recorded at a scan rate of 5 °C min^{-1}. Repeated heating and cooling of the samples were $\pm$ 1 kJ mol^{-1}, and a prolonged aging time of 8 h did not affect the results obtained. It was confirmed that gels were formed by opening the cups after the measurements.

Results

The gelation behavior for bisamide gelators **a2**−**a17** and bisurea gelators **u4**−**u18** were determined in a range of apolar and polar solvents, and for those cases where gelation was observed, the critical gelation concentration (cgc) was determined.[19,24−26] The cgc values for bisamide gelators **a2**−**a17** and bisurea gelators **u4**−**u18** are listed in Tables 1 and 2, respectively.

It is apparent from Table 1 that **a2**, the bisamide compound with the shortest tail (ethyl), is already a good gelator for many apolar solvents. In solvents consisting of linear or cyclic hydrocarbons, the cgc values are between 1.5 and 2.0 mg mL^{-1}, which corresponds to gelation at only 1.5 wt % of gelator. In more polar solvents, the cgc of **a2** increases; however, in solvents such as DMSO, gelation is inhibited, and precipitation or solubilization is observed.

For **a2**, the formation of intermolecular hydrogen bonds and interactions of the cyclohexyl rings are expected to be the major driving force for gelation, as the van der Waals interactions of the short alkyl tails are unlikely to contribute significantly. In solvents that interfere with hydrogen bond formation (e.g. alcohols), gelation is not observed, and **a2** is soluble at concentrations >20 mg mL^{-1}. Elongation of the alkyl tail by one methylene unit (i.e., **a3**) improves gelation (i.e., lower cgc values) in apolar solvents compared with **a2**; however, the gelation of polar solvents is again not observed. The same trends in gelation behavior are observed for remaining amide-based gelators **a5** to **a13**, with the exception of compound **a4**, which forms microcrystals in many of the apolar solvent examined. Compound **a4** has, as with **a2**, an odd number of methylene units in the alkyl tail in contrast to gelators **a3** to **a17**, which have an even number of methylene units. It might be related to an odd−even effect (i.e., there is a different orientation of the molecules in the packing for the compounds with an odd number of carbon atoms compared to those with an even number).[29−32] Compounds **a5**−**a13** are potent gelators of the apolar solvents and polar solvents tested that do not compete or compete only weakly for hydrogen

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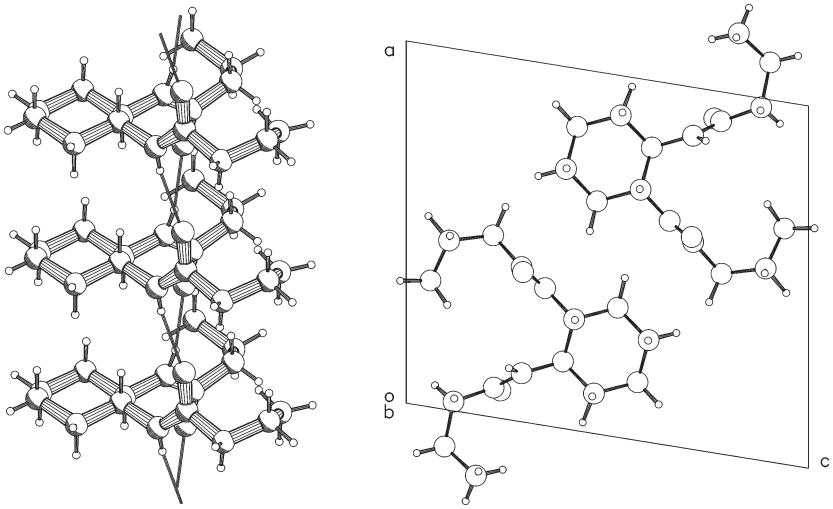

Figure 2. Drawing of the asymmetric unit cell of **a3** along the crystal lattice 010, showing the presence of intermolecular hydrogen bonding between the amide groups, positioned in an antiparallel fashion and a projection along the unit cell *b* axis.

bonding (e.g., 1,2-dichloroethane and *n*-butylacetate, Table 1).[33] In polar solvents that can compete strongly for hydrogen bonding (e.g., alcohols), gelation does not occur with the exception of **a11** in 1-propanol, which forms a gel at high gelator concentrations (>44 mg mL^{-1}), as demonstrated by Hanabusa et al.[24]

Where the alkyl tails of the bisamide gelators are longer (e.g., in **a15** and **a17**), gelation occurs in all apolar and in hydrogen bonding polar solvents (e.g., 1-propanol) at a low concentration of 2.5 mg mL^{-1}. In aliphatic and aromatic solvents, these compounds are potent gelators, and the cgc values are sufficiently low to classify them as supergelators (<0.5 wt %).[34] Overall, it is apparent that the elongation of the alkyl tail on the bisamide gelators leads to lower cgc, especially in polar solvents; however, the effect is much less pronounced in apolar solvents.[35−37]

The solubility of the bisurea-based compounds (e.g., **u4**) is much less than that observed for the bisamide gelators (e.g., **a4**), which is also substituted with two *n*-butyl tails. Compound **u4** is insoluble in most of the apolar solvents examined (Table 2). An increase in the alkyl tail length increases solubility, and compounds **u6** and **u8** are soluble at elevated temperatures in apolar solvents with gelation occurring upon cooling. However, in polar solvents these compounds precipitate upon cooling rather than form gels. For compounds **u10**−**u18**, in which the length of the alkyl tail is further increased, the gelation of polar solvents upon cooling is also observed, and these compounds form gels in all of the solvents examined.

Of the bisurea compounds with long alkyl chains tested, compound **u16** has, overall, the lowest cgc values, and it appears that this alkyl chain length is optimal. Indeed, the cgc values determined are sufficiently low enough to classify **u16** as a supergelator (0.5 wt %).[34]

X-ray Crystallographic Analysis of a3. As a consequence of the high anisotropy of the growth of crystals of the compounds examined in the present study, the needle-shaped crystals obtained were typically unsuitable for X-ray crystallographic analysis. However, suitable crystals were obtained for bisamide **a3** (Figure 2) by dissolving a small amount of **a3** in 1-propanol and allowing the solvent to evaporate slowly. The unit cell of **a3** has $P2_1$ symmetry and contains two molecules of **a3** (a = 11.776(2) Å, b = 4.777(1) Å, c = 13.250(3) Å and $\beta = 99.185(3)°$). In the crystalline state, the compounds arrange to form an infinite hydrogen-bonded chain along the *b* axis via the amide groups. The orientation of both amide groups in the molecule is antiparallel, and the two intermolecular hydrogen bonds are of differing lengths: 2.845(3) Å (N1−H21−O1, 170(3)°) and 2.855(3) Å (N2−H22−O2, 164(3)°).

The alkyl chains do not adopt an all-*trans* configuration, as shown by the torsion angles from C1−N1−C7 to C8−C9−C10 of 179.4(2)°, 128.5(3)°, and −64.8(4)° for one chain and from C6−N2−C11 to C12−C13−C14 of 175.4(2)°, −122.8(3)°, and 63.6(4)° for the second chain. Presumably, the chains are too short for an all-trans configuration to be energetically favorable. In addition, Figure 2 shows that there is a screw axis along the *b* axis, which leads to the formation of sheets.

Unfortunately, it was not possible to obtain crystals large enough for single-crystal X-ray analysis for any of the bisurea-based gelators. From crystals grown from **u6** in ethanol, it was possible to determine only, with considerable uncertainty, the unit cell symmetry: $P2_12_12_1$. From modeling studies on bisurea gelators[19] and the single-crystal structure of **a3**, it is apparent that both classes of gelators require hydrogen bonding units to be in an antiparallel conformation to achieve gelation.

The validity of the extrapolation of intermolecular structure in the crystalline state and the gel state was assessed by FTIR spectroscopy. FTIR spectroscopy is a powerful probe of hydrogen bonding interactions because several absorptions in the infrared region display distinct shifts upon hydrogen bonding.[38] In particular, the NH (stretch), amide I, and amide II vibrations are sensitive to changes in hydrogen bonding and hence aggregation. FTIR spectra of the gelators in solution were recorded to compare the position of the bands with those in the gel and crystalline state. In Tables 3 and 4, the positions of these bands are listed for the bisamide and bisurea gelators in different states. Unfortunately, because of the strong aggregation of the bisurea gelators only the solution spectra of compounds **u4**−**u12** could be obtained.

(33) The involvement of two distinct intermolecular interaction types with differing solvent dependence precludes a facile quantitative correlation to simplified solvent parameters such as solvent acceptor and donor numbers.

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Table 3. Selected FTIR Absorption Bands (ν, cm^{-1}) of Bisamide Gelators in Crystalline, Gel, and Solution States[a,b]

bisamide	state	NH (stretch)	amide I	amide II
a3	solution in CH_2Cl_2[c]	3430	1662	1514
a17	solution in CH_2Cl_2[c]	3429	1661	1514
a3	crystal[d]	3287	1639	1551
a3	decalin[c]	3280	1635	1549
a17	decalin[c]	3280	1637	1546
a7	DMSO[c]	3284	1636	1545
a17	DMSO[c]	3287	1637	1545
a15	1-propanol[d]	3279	1638	1546
a17	1-propanol[d]	3279	1638	1546

[a] For a complete overview, see Supporting Information. [b] Uncertainty (±2 cm^{-1}). [c] Recorded in a CaF_2 cell with 0.1 mm spacing and concentrations of < 1 mg/mL for solutions. [d] Recorded as an intimate mixture with KBr.

Table 4. Selected FTIR Absorption Bands (ν, cm^{-1}) of Bisurea Gelators in Crystalline, Gel, and Solution States[a,b]

bisurea	state	NH (stretch)	amide I	amide II
u4	solution in MeOH[c]	[e]	1656	1575
u12	solution in MeOH[c]	[e]	1652	1574
u6	crystal[d]	3331	1633	1603
u6	decalin[c]	3323	1632	1601
u18	decalin[c]	3327	1631	1595
u4	DMSO[c]	3332	1630	1604
u18	DMSO[c]	3337	1629	1611
u10	1-propanol[d]	3324	1633	1591
u18	1-propanol[d]	3329	1633	1590

[a] For a complete overview. see Supporting Information. [b] Uncertainty (±2 cm^{-1}). [c] Recorded in a CaF_2 cell with 0.1 mm spacing. [d] Recorded as an intimate mixture with KBr. [e] Region blocked by solvent absorption bands.

From the FTIR spectroscopic data, shown in Table 3, it is apparent that in CH_2Cl_2 solution the bisamide gelators do not aggregate because the NH stretch absorption (3429−3430 cm^{-1}) and the amide I absorption (1661−1662 cm^{-1}) appear at wavenumbers typical of non-hydrogen-bonded systems.[38] In the gel state, the bisamides are hydrogen bonded in apolar as well as polar solvents with the position of the bands shifted to values typical of hydrogen-bonded systems.[38] There are no large differences observed between the absorption band positions for the gelators of differing chain lengths, indicating similar hydrogen bonding in the gelators examined. Furthermore, the FTIR spectrum of **a3** in the crystalline state compares closely to the spectrum of **a3** in the gel state, indicating that in both states the compound is hydrogen bonded in a similar arrangement, justifying the comparison of the results of the single-crystal X-ray studies with those of the gels. There is a minor difference between the position of the amide II band in the crystalline state compared to that in the gel state, possibly because of the alkyl tail being more ordered in the crystalline state because this band is due to a combination of N−H bending and C−N stretching vibrations.

The position of the amide I band in methanol shows that these bisurea compounds are not aggregated in this solvent (Table 4).[38] However, in this solvent for bisureas with longer alkyl tails (e.g., **u16** and **u18**), precipitation was observed, showing the aggregative tendency of these compounds. The position of the absorption bands in the gels formed in the different solvents shows the presence of hydrogen bonds. Furthermore, in the crystalline state the molecules are aggregated via hydrogen bonding as was suggested by molecular modeling.[19] However, the relative contributions of hydrogen bonding and van der Waals interactions to the formation of the gel state could not be inferred from the FTIR spectra.

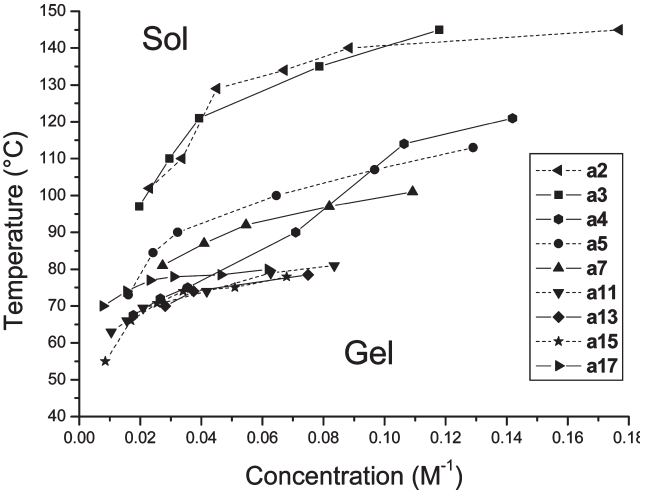

Figure 3. Gel−sol phase-transition curves of bisamide gelators **a2**−**a17** in decalin.

Thermal Stability. The effects of changing the relative contribution of hydrogen bonding and van der Waals interactions, together with the effect of the solvent on the thermal stability of the gel, were studied by the dropping ball method.[27] The T_{gs} of the gel was considered to be reached when the ball had reached the bottom of the vial. It should be noted that the gelator may not have been dissolved completely at this temperature.[39] Nevertheless, this technique provides a good indication of the thermal stability of the gel. By determining the T_{gs} of gels over a range of concentrations, the gel−sol phase-transitions curve of the gelator in a particular solvent can be plotted (e.g., Figure 3).[26]

An example of a plot of a gel−sol phase-transition curve for gelators **a2**−**a17** is provided in Figure 3. At low gelator concentrations, an increase in T_{gs} is observed with an increase in the concentration of gelator; however, this increase holds up only to a specific concentration.[26] In this solvent (decalin), all of the bisamide gelators tested were capable of forming gels. The gels of the bisamide gelator with the shortest alkyl chain, **a2**, have the highest gel−sol phase-transition temperature (> 140 °C at concentrations of > 70 mmol). The high thermal stability of gels of **a2** indicates that the high polarity is a major driving force for gelation in this solvent. Notably, the T_{gs} values for bisamide gelators at the same concentration decrease with increasing alkyl tail length. This decrease in T_{gs} reaches a minimum for **a13**, and for the bisamide gelator with the longest alkyl tail tested, **a17**, essentially similar T_{gs} values were found. The exception to this trend is **a4**, possibly due to an odd−even effect. The leveling off of the gel stability is counterintuitive because it would be expected that an increase in the length of the alkyl tail leads to an increase in the thermal stability due to larger van der Waals interactions. Most likely, the increased LMWG interactions achieved with longer alkyl chains are less important than the increase in molecular solubility in organic solvents. That is, the longer-tailed bisamide gelators are more soluble in decalin, and hence the decrease in the T_{gs} is observed.

In decalin, the T_{gs} values of the bisurea gels could not be determined reliably because they are > 130 °C. Above these temperatures, the urea group is unstable and decomposes.[40] Nevertheless, the high gel−sol phase-transition temperatures

(39) Hirst, A. R.; Coates, I. A.; Boucheteau, T. R.; Miravet, J,F.; Escuder, B.; Castalletto, V.; Hamley, I. W.; Smith, D. K. J. *Am. Chem. Soc.* **2008**, *130*, 9113–9121.

(40) Schaber, P. M.; Colson, J.; Higgins, S.; Thielen, D.; Anspach, B; Brauer, J. *Thermochem. Acta* **2004**, *424*, 131–142.

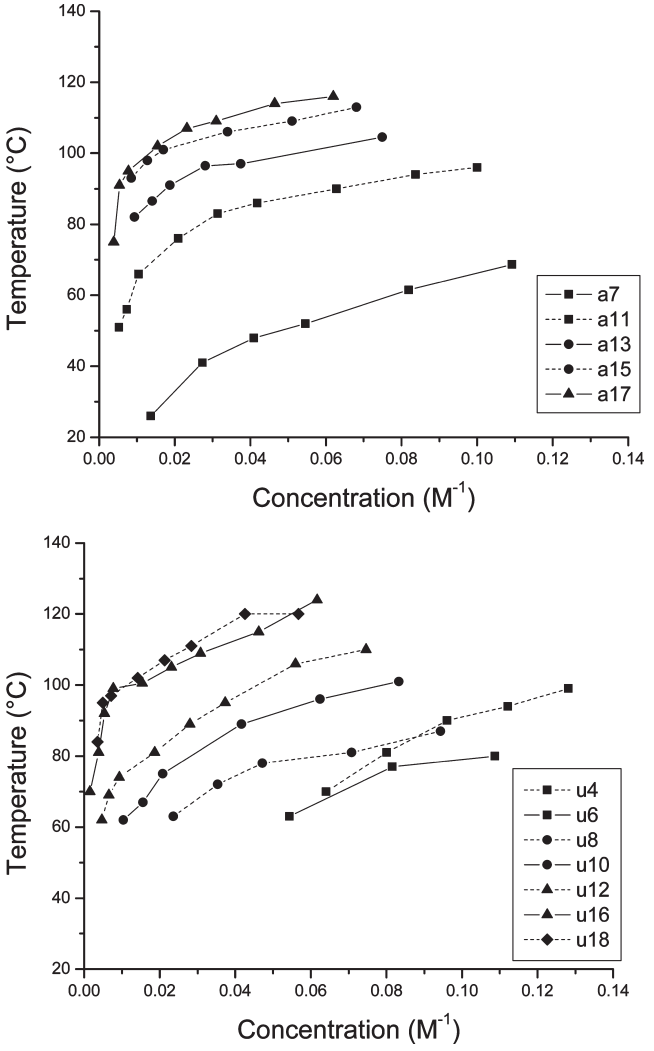

Figure 4. Gel−sol phase-transition curves of gel formed from bisamide gelators **a7**−**a17** and bisurea gelators **u4**−**u18** in DMSO.

confirm that in apolar solvents the thermal stability of the bisurea gels is higher than that of the bisamide gels. Most likely, the introduction of extra hydrogen bonding units leads to stronger gelator−gelator interactions within the fibers, together with less-favorable solvation in apolar solvents.

The gel−sol phase-transition curves of bisamides **a7**−**a17** and bisurea gelators **u4**−**u18** in DMSO are displayed in Figure 4. The T_{gs} of the gels shows an opposite trend to that observed in decalin. The melting temperatures (T_{gs} values) of the gels increase with increasing length of the alkyl tail of the gelator. The only exception to this trend is the melting temperature of **u4**, which is higher than that of **u6**. The T_{gs} values of the gels formed by **a15** and **a17** as well as **u16** and **u18** are essentially identical and show that the elongation of the alkyl substituents has a limited effect.

The gel−sol phase-transition curves of bisamide gelators **a15** and **a17** and bisurea gelators **u10**−**u18** in 1-propanol are shown in Figure 5. The other compounds examined do not form stable gels in this solvent (Tables 1 and 2). In 1-propanol, as was observed for DMSO, the stability of the gels increases with an increase in the length of the alkyl tail. The bisurea gelators behave in a more complex manner compared with the bisamide gelators. Compounds **u10** and **u12** have similar T_{gs} values; however, the thermal stability increases with the elongation of the alkyl chain, as observed for **u16** and **u18**. In both of these polar solvents, the increase in the thermal stability with elongation of the alkyl

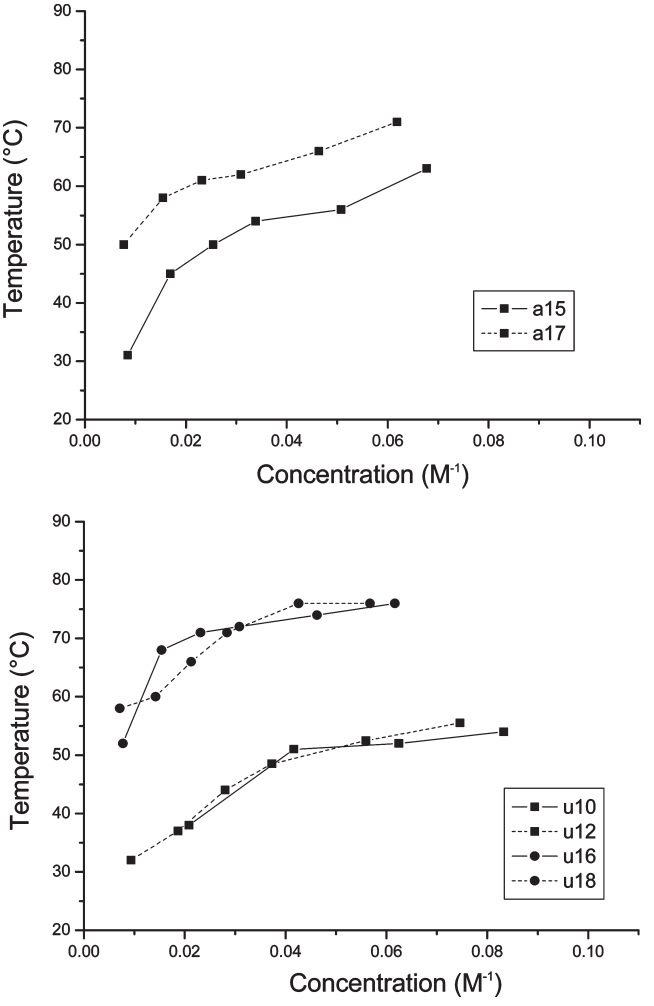

Figure 5. Gel−sol phase-transition curves of the gel formed from bisamide gelators **a15**−**a17** and bisurea gelators **u10**−**u18** in 1-propanol.

substituents is most likely due to increasing van der Waals interactions between gelator molecules together with less-favorable solvation in polar solvents.

More quantitative information regarding the melting of the gels was obtained from DSC measurements on native gels. In the heating traces, most of the bisurea gels exhibit multiple transitions in all three solvents investigated in this work (SOI). These multiple transitions are due to thermotropic polymorphism[41] as has been reported before for **u12**.[9] Because of this thermotropic polymorphism, a direct correlation between the DSC phase-transition temperatures and T_{gs} obtained from the dropping ball experiments was not observed. Nevertheless, the melting enthalpy (ΔH_m) of the gels can be obtained from the combined areas of the different phase transitions in the DSC traces. Figure 6 shows the melting enthalpies for the gels in the three investigated solvents as a function of the length of the alkyl chain (Figure 6). From these data, it can be concluded that for both the bisamide and bisurea gelators the ΔH_m of the gels increases with increasing molecular mass (i.e., increasing alkyl chain length). Furthermore, the ΔH_m of the gels of bisamide gelators in the polar solvents examined are much higher compared to those in apolar solvent decalin (5−25 kJ mol^{-1}, see also Supporting Information). Also,

(41) The thermotropic behavior of the bisurea gelators will be reported separately. Zweep, N.; Browne, , W. R.; Feringa, , B. L.; van Esch, , J. H., manuscript in preparation.

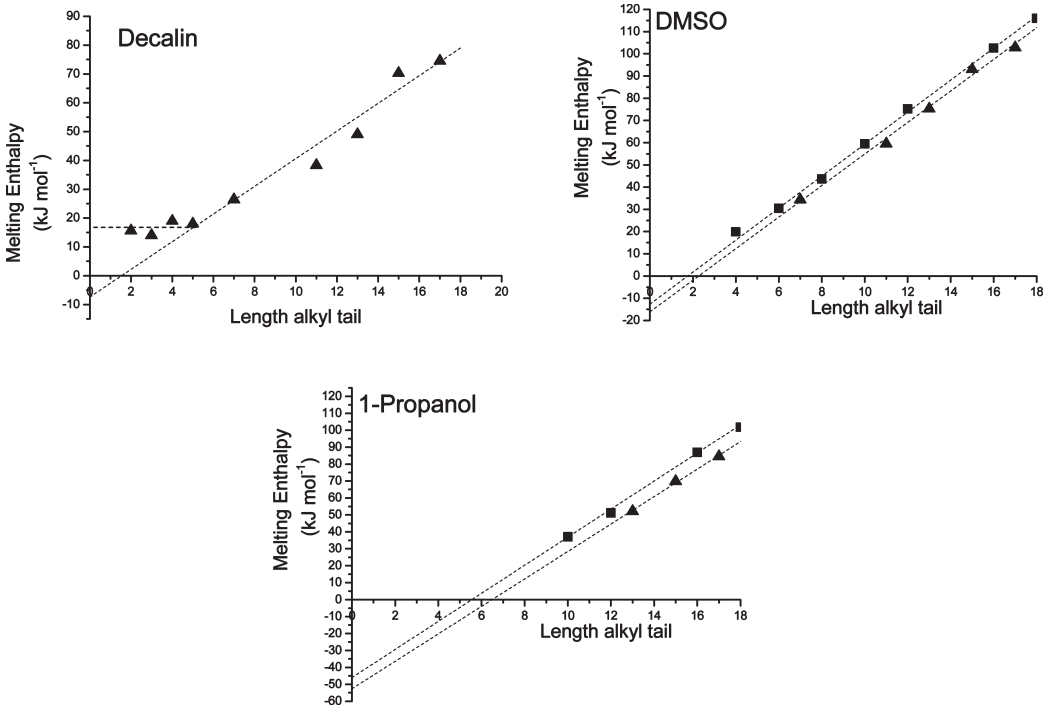

Figure 6. ΔH_m of the gel formed from the bisurea (■) and bisamide (▲) gelators in decalin, DMSO, and 1-propanol plotted against the length of their alkyl tails. The dashed line represents a linear fit.

in DMSO the melting enthalpies of the gels are higher compared to those in 1-propanol. The high melting temperatures of bisurea gelators in apolar solvents precluded the determination of their melting enthalpies. The low ΔH_m of the gels of bisamide gelators in decalin compared to ΔH_m of gels formed in the polar solvents examined is unexpected because one would expect that the hydrogen-bonding interactions in apolar solvents would be stronger. This points to a much lower relative contribution of the van der Waals interaction by the alkyl chain as a result of favorable solvation in apolar solvents.

In the plots of melting enthalpy against the length of the alkyl tail, a striking effect is observed; the melting enthalpy of the gelators is related linearly to the length of the alkyl tail. By fitting a linear function to the melting enthalpy, the increase in stability per increase in methylene unit can be determined (Supporting Information). In decalin, it was found that, for the bisamide, it increases by 2.2 kJ mol^{-1} ($\pm$0.1) per methylene unit. In the polar solvents examined, the alkyl tail provides the same contribution to the stability in both the bisamide and bisurea gelator systems, albeit with the contribution differing depending on the solvent: ca. 3.6 kJ mol^{-1} in DMSO and ca. 4.2 kJ mol^{-1} in 1-propanol. This indicates that the relative difference in the strength of the inter-gelator van der Waals interactions provided by the alkyl tails and the solvent−gelator van der Waals interactions is more pronounced in more polar solvents.

In 1-propanol and DMSO, the *x*-axis intercept of the linear fit provides an estimate of the minimum length of the alkyl tail required for aggregation in these solvents (i.e., $n = 6$ for 1-propanol and $n = 2$ for DMSO). These lengths are in good agreement with the results of the gelation experiments (Tables 1 and 2). Also, by extrapolation a more negative melting enthalpy for the core is found in 1-propanol compared to that in DMSO. For the bisamide core, it is found to be −52.6 kJ mol^{-1} in 1-propanol and −16.1 kJ mol^{-1} in DMSO. For the bisurea core, it is found to be −46.3 kJ mol^{-1} in 1-propanol and −12.7 kJ mol^{-1} in DMSO. This indicates that in 1-propanol the core is more soluble than in DMSO, most likely because 1-propanol acts as a hydrogen bond donor and acceptor whereas DMSO is only a hydrogen bond acceptor.[42] Furthermore, from these data the difference in stability between bisamide and bisurea gelators in these solvents is obtained, 6.3 kJ mol^{-1} in 1-propanol and 3.4 kJ mol^{-1} in DMSO in favor of the bisurea gelator. This shows that the ability of the urea group to form four hydrogen bonds compared to the two of the amide group provides for better thermal stability.

In decalin, bisamide gelators **a2**−**a5** do not hold the linear trend found in melting enthalpy for bisamide gelators. This suggest that the contribution of the alkyl chains to the stability of the gel via van der Waals interactions requires a length longer than $n = 6$. Most likely, below $n = 6$ the alkyl chains do not adopt an all-trans configuration in the assembled state as seen in the X-ray structure of **a3** and previously for lipids.[43] The comparable melting enthalpies of these gelators (ca. 16 kJ mol^{-1}) shows that the stability of the gels is governed solely by the bisamide core.

Discussion

For the gelation of solvents by low-molecular-weight molecules to occur, a combination of intermolecular interactions, which results in the anisotropic growth of supramolecular structures, is required. The specific contribution of each type of interaction as well as the influence of the solvent itself on gelation is still not fully understood, however.[3,4,17] In the present report, the gelation behavior of a series of bisamide- and bisurea-based low-molecular-weight gelators, built into a transoid cyclohexyl-diamine core with systematic variation in the length of the two linear alkyl moieties, is examined in a range of apolar and polar solvents in an attempt to understand the relative importance of the several contributions to anisotropic fiber growth and stability.

(42) Marcus, Y. *The Properties of Solvents*; Wiley: Chichester, U.K., 1998; pp 133−202, ISBN 0-471-98369-1.
(43) Oakes, R. E.; Beattie, J. R.; Moss, B.; Bell, S. E. J. *J. Mol. Struct.* **2002**, *586*, 91–110.

The combination of single-crystal X-ray analysis, dropping ball, DSC, and FTIR spectroscopy indicates that the relative contributions of the van der Waals and hydrogen-bonding interactions to gelation by the bisamide and bisurea LMWG are similar but not equal. The influence of solvent on the gelation behavior is apparent from the cgc values of the different gelators. It is tempting to correlate gelation properties such as the cgc values of these organogelators with known solvent parameters (e.g., solvent acidity and basicity). However, such a correlation with potentially relevant solvent parameters could not be identified, in contrast to other classes of low-molecular-weight gelators.[44] Most likely, this is due to the presence of two distinct motifs for anisotropic aggregation (i.e., hydrogen bonding and van der Waals interactions). The relative contribution of each motif change depends on the solvents employed; however, the two aggregation driving interactions are essentially independent of each other.

In comparison to the bisamide-based organogelators, the increased hydrogen-bonding ability in the bisurea gelator system reduces the solubility of the compounds in apolar solvents. The hydrogen-bonding ability is presumed to lead to too rapid an aggregation of the molecules in solution to allow for the formation of the 3D networks required for gelation. This effect is most pronounced for compound **u4**, where crystallization rather than gelation occurred in some of the apolar solvents examined. The increased gelation ability of the bisurea compounds in polar solvents shows that the contribution from the additional hydrogen bonds to gelator−gelator interactions in the gel fibers is more important than the solvation of these polar groups in polar solvents.

In polar solvents, however, van der Waals interactions provided by the alkyl chains are essential because gelation occurs only above a critical length of the alkyl chain formation in order to compensate for the favorable solvation of the polar bisamide and bisurea moieties. Elongation of the alkyl tail of the gelators leads to the further improvement of gelation properties in both apolar and polar solvents, albeit for different reasons. In polar solvents, the cgc, T_{gs} and ΔH_m values improve with increasing alkyl chain length, which is most likely due to both an increase in gelator−gelator interactions together with decreasing interactions of the apolar chains with polar solvent molecules. In apolar solvents, however, we observed an improvement in the cgc and ΔH_m but a decrease in the T_{gs} with increasing alkyl chain length. Most likely, the increase in gelator−gelator interactions with increasing alkyl chain length is compensated for by the increasingly favorable solvation of these apolar moieties in apolar solvents. These conclusions are consistent with the lower slopes of the ΔH_m alkyl chain length regressions in apolar decalin compared to those in polar DMSO and 1-propanol.

It is apparent that an increase in anisotropy through an increase in the length of the alkyl tail does not result in an improvement in the thermal stability of the gels of the apolar solvent (i.e., the melting enthalpy increased only marginally with increasing alkyl tail length). An increase in the hydrogen bonding strength, through replacement of the bisamide with a bisurea moiety, resulted in a substantial increase in the melting temperatures. In polar solvents, however, the increase in thermal stability and melting enthalpy with an increase in the length of the alkyl tail was dominant with the effect of variation of the hydrogen bonding unit being only marginal.

Conclusions

In the present study, the solvent dependence of the gelation properties of two series of bifunctional organogelators is described. We have demonstrated that for organogel-forming compounds in polar solvents van der Waals interactions play a dominant role whereas in apolar solvents hydrogen-bonding interactions dominate. The results demonstrate the key point that in understanding the dependence of gelation strength on both solvent properties and the anisotropy of intermolecular interactions it is essential to recognize that the primary interaction driving the assembly of the gel fiber is itself solvent-dependent. Hence, the development of design rules for the construction of LMWG molecules incorporating more than one anisotropic growth element must take into consideration the role of the solvent in determining which of the contributions is dominant. The corollary of this conclusion is that the direct relation of gelation strength to changes in solvent properties is not possible and more complex relationships should be considered.

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Supporting Information Available: Details of syntheses and experimental details, DSC and FTIR spectroscopic data, and single-crystal X-ray data for **a3**. This material is available free of charge via the Internet at http://pubs.acs.org.

(44) Hirst, A. R.; Smith, D. K. *Langmuir* **2004**, *20*, 10851–10857.